ABSTRACT

The consumption of dietary supplements such as flavonoids may reduce risk of many civilization diseases. Flavonoids are able to modulate the activity of cytochromes P450 (CYPs), xenobiotic-metabolising phase I enzymes of biotransformation that are involved in the activation and detoxification of food-derived carcinogens. Inhibition of CYP activities by flavonoids has been extensively studied because of their potential use as agents blocking the initiation stage of carcinogenesis. On the other hand, flavonoids have been shown to enhance the activation of carcinogens and/or influence their metabolism *via* induction of specific CYPs. In the first part of this study, flavonoids dihydromyricetin and α-napthoflavone were explored for their possible effects on CYP1A1 expression and activity when administered in combination with carcinogen benzo[a]pyrene (BaP). For this purpose, liver, small intestine and colon microsomal fractions were isolated from treated rats and induction of CYP1A1 was evaluated by immunodetection and EROD activity measurements. In liver and small intestine, all combinations of BaP and flavonoids led to strong induction of CYP1A1 expression. Moreover, the CYP1A1 protein levels were almost identical to levels observed when the rats were treated with BaP alone. However, in comparison with BaP administered alone, the CYP1A1 activities significantly decreased in most of the cases when also one of the flavonoids was present. This would suggest that the selected flavonoids could be capable of reducing the potential risk of cancer development.

In addition to their involvement in activation and inhibition of CYPs, dietary flavonoids can potentially also influence phase II enzymes of biotransformation. To be able to explore whether *N*-acetyltransferases (NATs) as representatives of phase II enzymes can be modulated by flavonoids, basic methods for detection and activity measurements need to be established. Thus, the second part of this study focused on introduction and optimisation of NAT immunodetection and specific NAT activity assay. Although 3 different chicken antibodies against human/rat NATs were prepared, none of them was able to detect NATs in rat cytosol mixture. NAT activity assay based on determination of CoA amount formed during reaction of the enzyme with specific substrate was first optimised using recombinant NATs. Subsequent attempts to measure the NAT activity in rat cytosols were successful.
Nevertheless, many optimisation steps still need to be performed.

Key words: flavonoids, cytochromes P450, *N*-acetyltransferase